衞生防護中心
Centre for Health Protection

Scientific Committee on Vector-borne Diseases

Options for Control of JE in Hong Kong

Purpose

Against the background of an increased number of JE cases in Hong Kong this year, it is imperative to consider and review the current strategies for JE control. This paper discusses the different options available with a view to facilitate discussion and recommendations on an overall strategy for JE control.

Options for control and criteria for appraisal

2. JE could be prevented by a combination of strategies which interrupts the natural transmission cycle of the virus. Each method has its own merits and limitations and should be considered against such criteria as effectiveness, safety, sustainability, and feasibility of implementation.

Human vaccination

3. Humans are dead-end hosts in the JE transmission cycle. Man is less frequently bitten by the vector and not bitten in large numbers until the density of the infected vector is maximal. As such, infections in humans are generally preceded by that in amplifying animals and infectious mosquitoes are relatively rare until amplification has occurred in pigs (1).

4. Effective JE vaccines for human are available and its extensive use in national childhood immunization programmes has contributed to the reduction of cases in JE endemic countries. The mouse-brain derived JE vaccine (the only internationally accepted JE

vaccine) is associated with adverse neurological and allergic reactions. The estimated rate of moderate to severe neurological adverse reactions was 1-2.3 per million vaccinations. Hypersensitivity reactions occurred in 0.6% of vaccinations. In Hong Kong, vaccination is currently only recommended for travelers to endemic areas especially staying in rural areas for 4 weeks or longer. The recommendation was based on consideration of local epidemiology, and weighing the potential risks against the benefits of vaccination. The need to vaccinate special groups who might be exposed to a higher risk of infection is being considered (see SCVBD Paper 10/2004).

Vector Control

5. The Culex tritaeniorhynchus mosquito is the main vector found in Hong Kong.Studies have shown that epidemics of human infection follow the peak isolation rate of the virus in mosquitoes by 17-20 days. JE vector control by chemical insecticide spraying could effectively reduce vector density. However, the long flight range of Culex tritaeniorhynchus mosquito meant that large treatment radius is needed to attain good coverage. Development of insecticide resistance is another concern. These issues have raised questions as to the sustainability of this method for JE control if used alone (1, 2).

Swine vaccination

6. Pigs are the major amplifying host for JE transmission. They have a high birth rate which provides susceptibles for ongoing transmission and respond to infection with a high and sustained level of viraemia that can infect mosquitoes. Because of their high body temperature and large hairless body surface area, they are able to attract thousands of mosquitoes nightly. When placed in the field as sentinel animals to monitor transmission of JE, pigs are infected rapidly, usually within several weeks, just before or as human transmission commences (2).

7. A study in Indonesia showed that the difference in seroprevalence of JE antibodies in two villages was directly correlated to the pig population (3). An epidemiologic survey in India demonstrated the seroconversion in sentinel farm animals followed by sero-conversion and illness in human population (1). In Taiwan, human cases of JE often follow 2-3 weeks after seropositivity rates in pigs reached 50% (Report on visit to Taiwan on JE, August 2004). During the 1970s, nationwide surveillance of swine infected by JE in Japan revealed that the number of human patients infected by JE increased as the number of pigs infected by the virus increased on the whole (4). In Singapore, the elimination of pig farming to make way for urbanization resulted in a drastic reduction in incidence of JE (5).

8. Since epidemic human diseases of JE have rarely occurred in the absence of swine, it has been hypothesized that vaccination of swine may

reduce rates of human disease (2). Swine vaccination was brought into operation to control JE virus transmission in several areas in Japan in the 1960s and 1970s. Field studies had demonstrated that swine vaccination contributed to the reduction of JE transmission in nature in Iki Island in Nagasaki Prefecture and in Kumamoto Prefecture (6,7,8). Findings from these and other studies are summarized in the Annex.

9. Despite being effective in the control of JE transmission, swine immunization has generally not been used as a principal method to control human JE in neighboring endemic countries for a number of reasons. For instance, the number of pigs to be vaccinated every year is large due to high turn-over rates. Timing for immunization is also a concern due to the presence of maternal antibodies interfering with live-attenuated vaccines and the absence of obvious seasonal patterns of JE transmission in tropical areas (2). In these countries, swine vaccination is usually done more for preventing abortion and stillbirth among breeder pigs. Some authors also cited the potential risk of recombination between vaccine virus and other wild-type flaviviruses (9).

Measures targeting birds and other animals

10. Bird-mosquito cycles are thought to be important in maintaining and amplifying JE virus in nature. Birds have been shown in experiments to develop sufficient viraemia to infect mosquitoes. They are seen as part of the enzootic virus cycle, especially in areas where swine are absent (2). Since experimental infection of horses, cattle and dogs induces low-level or no viraemia, these animals are considered as dead-end hosts in the enzootic cycle (2). No documentation has been identified on the use of strategies which target at birds to control the transmission of JE.

Advice sought

11. Members are invited to note the contents of this paper and discuss on the possible strategies for enhancing the control of JE in Hong Kong, taking into consideration the merits and disadvantages of each method.

Centre for Health Protection
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ANNEX

Summary of Japanese Studies on Swine Vaccination@

Place	Method	Results	Interpretation
Nagasaki Prefecture Karako and Aite (1966)	Vaccinated group: Karako area Control group: Aite area All the swine of the Karako area were immunized 2 to 3 times with commercially available inactivated JE vaccine for veterinary use.	• Haemagglutination inhibition (HI) test performed on randomly selected vaccinated swine showed 70% seroconversion; 30% remained seronegative • HI titre following vaccination was lower than titres elicited by natural infection • Virus isolation from *Cx tritaeniorhynchus* between June and August (just before appearance of infected mosquitoes to just after the disappearance of infected mosquitoes) found that the highest infection rate of the mosquito pools was 25% in the vaccinated area and 60% in the control area. Average infection rate in the vaccinated area was 6.3%; control area was 14.6% • The following year when swine vaccination was not carried out, the highest infection rate of mosquito pools was 100% in Karako and 80% in Aite.	The data indicated that JE virus transmission was reduced by swine immunization

Place	Method	Results	Interpretation
Nagasaki Prefecture Iki Island (1967-1972)	All swine vaccinated simultaneously by single inoculation of live-attenuated vaccine. As small numbers of swine persisted as potential amplifier hosts besides other animal species, two immunizations were given with a 1-month interval (June –July) from 1971 onwards	▪ HI test showed relatively lower titre antibodies persisted among vaccinated swine indicating absence of a booster effect due to natural infection ▪ HI titres among bovine sera were low indicating low frequency of natural infection ▪ Multiple JE virus strains isolated from field-caught *Cx tritaeniorhynchus* in each year between 1967-1970, but none in 1972; although the number of mosquitoes caught was also lower than the preceding 4 years ▪ No human JE case was reported in 1971; the number of human JE cases and deaths was reduced to less than 1 per year after swine vaccination implemented	Although there was no control area to compare, the number of human cases in the island was significantly reduced in ensuing years
Osaka Prefecture Takatsuki City and Ibaraki City (1967)	Swine immunization with inactivated JE vaccine for human use fortified to contain 3 times the usual amount of immunogen. A total of 1318 swine received 3094 inoculations	Virus infection rate of field-collected mosquitoes was 5.1% in vaccinated area, in contrast with 16.6% in the control area ($p<0.01$)	Swine immunization reduced JE virus transmission effectively

Place	Method	Results	Interpretation
Osaka Prefecture Yokosyoji, Higashi-Osaka City (1975)	Single-dose live attenuated JE vaccine given to weanling litter-mates of four months old bred together in the same pen Five pigs were vaccinated, 4 pigs served as controls	▪ Vaccinated pigs developed antibodies within one week after vaccination ▪ Antibody titres were lower than that in control group naturally infected with JEV ▪ No virus was isolated from the all the vaccinated pigs, but virus was isolated from all 4 control pigs; duration of viremia in control pigs varied from 1-4 days	No virus was isolated from vaccinated pigs despite their antibody titres being lower than that of the control group after natural infection; this indicates a booster effect of natural infection in the vaccinated group without any manifestation of viremia, and the effectiveness of the vaccine in blocking the *Culex*-swine cycle of JE virus amplification
Kumamoto Prefecture (1985) Background: After a significant reduction in the number of human JE cases in Japan, substantial numbers still occurred in this Prefecture, accounting for 10-57% of all JE cases in the whole of Japan between 1978-84	Implementation of a swine immunization programme in 1985 in Kumamoto City and 10 surrounding township areas with a live-attenuated JE vaccine.	▪ Number of human cases in vaccinated areas reduced from 10 in 1984 to 1 in 1985 ▪ Appearance of IgM antibodies in swine was delayed and reduced in the vaccinated areas compared with unvaccinated areas	Swine vaccination has contributed to the reduction of JE transmission in nature

Place	Method	Results	Interpretation
Kyoto City (1968-1970)	Live attenuated JE vaccine was used to immunize swine in mid to late June	▪ Infection rates of mosquitoes caught in pig-pens housing the vaccinated swine were lower and the appearance of infected mosquitoes was delayed as compared with control group ▪ Vaccinated swine produced lower titres of HI antibodies (1:20 to 1:40)	There is augmentation of HI antibodies in vaccinated swine after natural infection

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